UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/325,278	10/26/94	BJORCK	L 216764

18M1/0325

KARL R. HERMANS
SEED AND BERRY
701 FIFTH AVENUE
SEATTLE WA 98104-7092

EXAMINER	
CAPUTA, A	
ART UNIT	**PAPER NUMBER**
1817	

DATE MAILED: 03/25/97

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/325,~~746~~ 178	Applicant(s) Bjorck et al.
	Examiner Anthony C. Caputa	Group Art Unit 1817

☒ Responsive to communication(s) filed on *Feb 18, 1997*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1, 3-5, and 11-13* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 3-5, and 11-13* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☒ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *4*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Specification

1. The following guidelines illustrate the preferred layout and content for patent applications. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

The following order or arrangement is preferred in framing the specification and, except for the title of the invention, each of the lettered items should be preceded by the headings indicated below.

(a) Title of the Invention.
(b) Cross-References to Related Applications (if any).
(c) Statement as to rights to inventions made under Federally-sponsored research and development (if any).
(d) Background of the invention.
    1. Field of the Invention.
    2. Description of the Related Art including information disclosed under 37 CFR 1.97-1.99.
(e) Summary of the Invention.
(f) Brief Description of the Drawing.
(g) Description of the Preferred Embodiment(s).
(h) Claim(s).
(i) Abstract of the Disclosure.

2. Sequence rules set forth in 37 C.F.R. § 1.821 require the use of SEQ ID No if the sequence is embedded in the text or in the claims. All sequences must be referred to by use of an identifier such as "SEQ ID NO" as presented in the Sequence Listing even though the sequence itself may be imbedded in the text of the application.

The disclosure and/or claims (see pages 16, 23, and 25 of the specification) of the application mention a sequence that is set forth in the Sequence listing but reference is not properly made to the sequence by the use of a sequence identifier in the text.

3. The disclosure is objected to because of the following informalities:

The specification makes reference to claims (i.e. see page 9, line 15).

The specification has misspelled DNA on page 9, line 16; page 10, line 29; and page 29, line 27.

The specification has misspelled Na Acetate on page 26, line 20.

The specification has misspelled Peptococcus on page 9, lines 13 and 14.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

5. Claim 1 is rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter.

With regard to claim 1 the protein has the same characteristics and utility as protein found naturally and therefore does not constitute as patentable subject matter.

In the absence of the hand of man, naturally occurring proteins are considered non-statutory subject matter. Diamond v. Chakrabarty, 206 USPQ 193 (1980). Mere purity of naturally occurring product does not necessarily impart patentability. Ex parte Siddiqui 156 USPQ 426 (1966). However when purity results in new utility, patentability is considered. Merck Co. v. Chase Chemical Co. 273 F. Supp 68 (1967). See also American Wood v. Fiber Disintegrating Co., 90 US 566 (1974); American Fruit Growers v Brogdex Co. 283 US 1 (1931); Funk Brothers Seed Co. v. Kalo Innoculant Co. 33 US 127 (1948). Filing of evidence of a new utility imparted by the increased purity of the claimed invention and amendment to the claims to

recite the essential purity of the claimed proteins is suggested to obviate this rejection. For example, "A purified protein...".

The recitation of the term "man-made", "synthetic", or "recombinant" to the claim fails to impart an character to the peptide which one of skill in the art could recognize and find protection from infringing the instant claims based thereupon" The law is well settled that while a product by process claim is limited and defined by the process of determination of patentability is based on the product itself. In re Brown, 459 F. 2d 531, 535, 173 USPQ 685, 688 (CCPA 1972), as cited in In re Thorpe, 77 F. 2d 695, 227 USPQ 964 (CAFC, 1985).

Double Patenting

6. The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1, and 11-13 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 4,876,194. Although the conflicting claims are not identical that is the instant application sets forth the amino acid sequence of protein L, in contrast to the issued patent they are not patentably distinct from each

other because the claims of the instant application and the issued patent broadly encompass protein L, subfragments thereof, a kit and pharmaceutically acceptable carrier comprising said protein. Furthermore, it is reasonable to conclude protein L as set forth in the issued patent is the same, or in the alternative an obvious or analogous variant of protein consisting of SEQ ID No. 1 as recited in the instant application since they have the same properties (useful as kit, useful as pharmaceutical composition, bind light chains of immunoglobulins, and from P. Magnus strain 312).

8. Claims 3-5 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 4,876,194 in view of Guss et al. (WO 87/05361)(Art Cited by Applicants in the IDS) and Kastern et al. (1990) (Infection and Immunity 58(5):1217-22 5/90) (Art Cited by Applicants in the IDS).

'194 disclosure of the claimed invention is set forth above. '194 does not claim linking protein L to protein G or the C1, or C2 domains of protein G.

Kastern et al 1990 teach that since protein L reacts with light chains of immunoglobulin it reacts with all classes of immunoglobulin unlike other proteins such as proteins A or G (see page 1221: Column 1).

Guss et al. (WO 87/05361) teach protein G can be used as a method to isolate antibodies (see pages 1 and 2). Guss et al. teach that C1, C2, and C3 regions of protein G are the coding regions for IgG binding (see page 4). Guss et al teaches of fusing protein G with other proteins such as protein A (see page 5).

Guss et al. does not teach of linking protein L to protein G or the C1, or C2 domains of protein G as claimed. Nevertheless, it would have been obvious to one of ordinary skill in the art at the time of the invention to link protein L as recited by US Patent 4,876,194 with protein G or the C1, C2, C3 domains as set forth by Guss et al since as taught by Kastern et al 1990 protein L reacts with all classes of immunoglobulin unlike protein G.

Claim Rejections - 35 USC § 112

9. Claims 3, and 11-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3, and 11-13 are rejected since it not clear what constitutes as a "domain which bind to heavy chains in immunoglobulin G". Does a domain consist of a portion of protein, carbohydrate, or other product? Or in the alternative, does a domain consist of a fraction of composition which binds to the heavy chains of immunoglobulin G?

Claims 11-13 are rejected for being vague and indefinite since a composition comprises two or more products.

10. Claims 1, 3-5, and 11-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: 1.) protein L having (e.g. consisting) the sequence as set forth in SEQ ID No:1 (i.e. claim 1); and 2.) Protein LG having the sequence as set forth in SEQ ID No: 3 (i.e. claim 5) does not reasonably provide enablement for "variants", "subfragments"; "multiples or mixtures of the domains B1-B5" as recited. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (see Burgess et al.). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduce the biological activity of the mitogen (see Lazar et al.). These references demonstrate that a even a single amino acid

substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of a protein. In view of the lack of guidance, lack of examples, and lack of predictability associated with regard to producing and using the myriad or derivatives encompassed in the scope of the claims one skilled in the art would be forced into undue experimentation in order to practice broadly the claimed invention.

The problem of ascertaining functional aspects of the protein and determining what changes can be tolerated with respect thereto is extremely complex and well outside the realm of routine experimentation. While recombinant and mutagenesis techniques are known, it is **not** routine in the art to screen for positions within the protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining similar activity/utility are limited in any protein and the result of such modifications is unpredictable based on the instant disclosure (see Bowie et al., Science, Vol 247, pp 1306-1310, especially p. 1306, column 2, paragraph 2). One skilled in the art would expect any tolerance to modification shown for a given protein to diminish with each further and additional modification, e.g. multiple deletions. The sequence of some proteins is highly conserved and one skilled in the art would not expect tolerance to any amino acids modification in such proteins.

The specification does not support the broad scope of the claims which encompass a multitude of polypeptides because the specification does **not** disclose the following :

- the general tolerance to modification and extent of such tolerance;
- specific positions which can be predictably modified; and
- the specification provide insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have **not** provided sufficient guidance to enable one skilled in the art to make and use the claimed products in manner reasonably correlated with the scope of the claims broadly including any number of deletions, substitutions, additions, and fragments of any size. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re

Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made and still maintain activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 U.S.P.Q. 546 (Bd. Pat. App. & Int. 1986).

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1, and 11-13 are rejected under 35 U.S.C. 102(a) as being anticipated by Kastern et al. 1992 (J. Biol. Chemistry 267(18):12820-25 1992 (Art Cited by Applicants in the IDS)).

Kastern et al. 1992 disclose a protein L and subfragments with immunoglobulin binding activity. Kastern et al. disclose the protein and fragments thereof capable of binding light chains of immunoglobulins (see page 1283). Since the claimed invention broadly encompasses variants, subfragments, of protein L consisting (e.g. having the) of the amino acid sequence SEQ ID NO.1 and both the protein L as recited and set forth by Kastern et al. are capable of binding light chains of immunoglobulins the claimed invention is anticipated over the disclosure of Kastern et al. Kastern et al discloses the purified protein L and fragments were in a solution comprising 20 mM TRIS-HCl (see page 12821; Column 1) .

Kastern et al does not characterize the composition as a reagent kit or pharmaceutical composition. However, since the intended use of said composition does not carry any patentable weight and the composition as recited is disclosed by Kastern et al., the claimed invention drawn to a reagent kit or pharmaceutical composition as set forth in the claimed invention is anticipated over the disclosure of Kastern et al.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a certified translation of said papers has not been made of record. See MPEP § 201.15.

13. Claims 1 and 11-13 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 0 255 497 (Art Cited by Applicants in the IDS).

EP 0 255 497 disclose a protein L and subfragments with immunoglobulin binding activity (see title). EP 0 255 497 disclose the protein is capable of binding light chains of immunoglobulins (see claim 1). EP 0 255 497 disclose of a reagent kit and pharmaceutical composition comprising said protein L and subfragments thereof (see claims 10 and 11). EP 0255 497 does not characterize the protein as having the amino acid sequence as set forth in SEQ ID No.1. Nevertheless since the claimed invention broadly encompasses variants, subfragments, of protein L consisting (e.g. having the) of the amino acid sequence SEQ ID NO.1 and both the protein L as recited and set forth by EP 0 255 497 are capable of binding light chains of immunoglobulins the claimed invention is anticipated over the disclosure of EP 0 255 497.

14. Claims 1 and 11-13 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent No. 4,876,194 ('194) (Art Cited by Applicants in the IDS).

'194 discloses a protein L and subfragments with immunoglobulin binding activity (see abstract). '194 discloses the protein is capable of binding light chains of immunoglobulins (see Column 1). '194 discloses a reagent kit and pharmaceutical composition comprising said protein L and subfragments thereof with a pharmaceutically acceptable carrier, excipients and adjuvants (see claims 13 and 14 and Column 1). '194 does not characterize the protein as having the amino acid sequence as set forth in SEQ ID No.1. Nevertheless, since 1) the claimed invention broadly encompasses variants, subfragments, of protein L consisting (e.g. having the) of the amino acid sequence and 2) both the protein L as recited and set forth by '194 are capable of binding light chains of immunoglobulins the claimed invention is anticipated over the disclosure of '194.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0 255 497 (Art Cited by Applicants in the IDS) and further in view of Kastern et al. 1990 (Infection and Immunity 58(5):1217-22 5/90) (Art Cited by Applicants in the IDS) and Guss et al. (WO 87/05361) (Art Cited by Applicants in the IDS).

EP 0 255 497 disclosure is set forth above. EP 0 255 497 does not teach of linking protein L to protein G or the C1, C2 domains of protein G.

Kastern et al 1990 teach that since protein L reacts with light chains of immunoglobulin it reacts with all classes of immunoglobulin unlike other proteins such as proteins A or G (see page 1221: Column 1).

Guss et al. (WO 87/05361) teach protein G can be used as a method to isolate antibodies (see pages 1 and 2). Guss et al. teach that C1, C2, and C3 regions of protein G are the coding regions for IgG binding (see page 4). Guss et al teaches of fusing protein G with other proteins such as protein A (see page 5).

Guss et al. does not teach of linking protein L to protein G or the C1, or C2 domains of protein G as claimed. Nevertheless it would have been obvious to one of ordinary skill in the art

at the time of the invention to link protein L as taught by EP 0 255 497 with protein G or the C1, C2, C3 domains as set forth by Guss et al since as taught by Kastern et al 1990 protein L reacts with all classes of immunoglobulin unlike protein G.

17. Claims 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kastern et al. 1992 (J. Biol. Chemistry 267(18):12820-25 1992 (Art Cited by Applicants in the IDS)) and Guss et al. (WO 87/05361)(Art Cited by Applicants in the IDS).

Kastern et al. 1992 disclosure is set forth above. Kastern et al does not teach of linking protein L to protein G or the C1, C2 domains of protein G.

Kastern et al 1992 teach protein L has a broader Ig binding activity than protein G (see Introduction).

Guss et al. (WO 87/05361) teach protein G can be used as a method to isolate antibodies (see pages 1 and 2). Guss et al. teach that C1, C2, and C3 regions of protein G are the coding regions for IgG binding (see page 4). Guss et al teaches of fusing protein G with other proteins such as protein A (see page 5).

Guss et al does not teach of linking protein L to protein G or the C1, C2 domains of protein G as claimed. Nevertheless, it would have been obvious to one of ordinary skill in the art at the time of the invention to link protein L as taught by Kastern et al. 1992 with protein G or the C1, C2, or C3 domains as set forth by Guss et al. since as taught by Kastern et al 1992 protein L has a broader Ig binding activity than protein G.

18. Claims 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 4,876,194 ('194) (Art Cited by Applicants in the IDS) and Guss et al. (WO 87/05361) (Art Cited by Applicants in the IDS).

'194 disclosure is set forth above. '194 does not teach of linking protein L to protein G or the C1, C2 domains of protein G.

'194 teach protein L binds all Ig classes from different animal species (see Column 1).

Guss et al. (WO 87/05361) teach protein G can be used as a method to isolate antibodies (see pages 1 and 2). Guss et al. teach that C1, C2, and C3 regions of protein G are the coding regions for IgG binding (see page 4). Guss et al teaches of fusing protein G with other proteins such as protein A (see page 5).

Guss et al does not teach of linking protein L to protein G or the C1, C2 domains of protein G as claimed. Nevertheless it would have been obvious to one of ordinary skill in the art at the time of the invention to link protein L as taught by '194 with protein G or the C1, C2, or C3 domains as set forth by Guss et al since as taught by '194 protein L binds all Ig classes from different animal species.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Anthony C. Caputa, whose telephone number is (703)-308-3995. The examiner can be reached on Monday-Thursday from 8:30 AM-6:00 PM. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703)-308-0196.

Papers related to this application may be submitted to Art Unit 1817 by facsimile transmission. The faxing of such papers must conform with the notice published in the official Gazette 1096 OG 30 (November 15, 1989). The Fax number is (703)-308-4242

Anthony C. Caputa, Ph.D.

March 13, 1997

ANTHONY C. CAPUTA
PRIMARY EXAMINER
GROUP 1800